

**REMARKS**

Claims 1-3, 11-12, 15-19, and 24-25 were pending in the application. Claims 1, 2, 3, 17 and 25 have been amended by the amendments presented herein. Accordingly, after the amendments presented herein have been entered, claims 1-3, 11-12, 15-19, and 24-25 will remain pending.

Support for the amendments to the claims can be found throughout the specification and claims as originally filed.

*No new matter has been added.* Any amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and were done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

***Prolonged and Piecemeal Prosecution Of The Present Case***

Applicants object to the prolonged and piecemeal prosecution of the present application. The Manual of Patent Examining Procedure provides that "[p]iecemeal examination should be avoided." M.P.E.P. §707.7(g). In the present case, the Examiner had indicated in the Office Action dated May 14, 2004 that claims 1-3 and 25 were allowable. The claims, when indicated as allowable, were directed to methods of identifying compounds that bind to and/or modulate the activity of a Kv4.2 or Kv4.3 potassium channel by contacting a PCIP polypeptide with a test compound, and determining whether the test compound binds to and/or modulates *any* activity of the PCIP polypeptide. On October 13, 2004, during a telephone conference with the Examiner, the Examiner requested that the claims be amended to incorporate the specific activities of the 9q PCIP polypeptide described in the specification and indicated that such amended claims would be allowable. In the Amendment and Response filed on October 14, 2004, Applicants amended claims 1, 3, and 25 as requested by the Examiner to incorporate into the claims the specific activities of the 9q PCIP polypeptide that were explicitly taught in the specification. After making the claim amendments requested by the Examiner, the Examiner is now rejecting these claims in the present Office Action as not complying with the enablement requirement of 35 U.S.C. §112, first paragraph.

The Examiner's inconsistent and piecemeal examination of the present case is unfair to Applicants and contrary to United States Patent and Trademark Office practice and policy.

***Rejection of Claims 1-3, 11-12, 15-19, and 24-25 Under 35 U.S.C. § 112, First Paragraph***

The Examiner has rejected claims 1-3, 11-12, 15-19 and 24-25 under 35 U.S.C. § 112, first paragraph because, “[t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.” Specifically, the Examiner is of the opinion that

the specification, while being enabling for a method of identifying a compound which binds to Kv4.2 or Kv4.3 and/or modulates the potassium channel activity of Kv4.2 or Kv4.3; or a method of identifying a compound which binds to Kv4.2 or Kv4.3 and/or modulates the regulation of Ito, or peak current amplitudes or inactivation time constants does not reasonably provide enablement for a method of identifying a compound which binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel, or a method of identifying a compound which binds and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by contacting a biologically active PCIP polypeptide fragment, wherein the PCIP activity is regulation of the phosphorylation state of a potassium channel or portion thereof; regulation of the association of a potassium channel or portion thereof with the cellular cytoskeleton; regulation of the phosphorylation state of a potassium channel or portion thereof; regulation of the association of a potassium channel or portion thereof with the cellular cytoskeleton.

The Examiner also argues that,

the activities indicated as not being enabled are directed to methods using portions of potassium channel polypeptides, and thus the claims encompass methods using variant proteins. Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions.

Applicants traverse this rejection for the following reasons.

As an initial matter, Applicants wish to bring to the Examiner’s attention the fact that the currently rejected claims were indicated as allowable by the Examiner in the previous Office Action. The allowable claims were directed to methods of identifying a compound that modulates the activity of a Kv4.2 or Kv4.3 potassium channel by contacting a 9q PCIP polypeptide, or a cell expressing the 9q PCIP polypeptide, with a test compound and determining whether the test compound binds to and/or modulates **any** activity of the 9q PCIP polypeptide. After a telephone conference with the Examiner, Applicants amended the claims to

recite the *specific* activities of the 9q PCIP polypeptides that could be modulated, thereby *narrowing* the scope of the allowable claims. The limitations that were added to the claims are fully supported by the specification and the Examiner indicated during the telephone conference that the narrowing amendment requested by the Examiner would result in the claims remaining allowable. Therefore, the instant rejection is contrary to the previous indication of the claims as allowable, and to the Examiner's statements made during the telephone conference.

Notwithstanding the foregoing, Applicants respectfully submit that based on the teachings provided in Applicants' specification and the knowledge available to one of skill in the art, the ordinary skilled artisan would be able to make and use the claimed invention using only routine experimentation. Contrary to the Examiner's assertion, the specification does teach one of skill in the art how to make and use the claimed invention. Specifically, Applicants provide detailed teachings regarding the biologically active PCIP peptide fragments. For example, (and as detailed in previous responses) Applicants provide detailed teachings about the characteristics and location of EF domains, Kv4.3 or Kv4.2 potassium channel  $\alpha$  subunit binding domains, and C-terminal core domains of the 9q PCIP polypeptides. Based on the general knowledge in the art (as evidenced by, for example, Scannevin *et al.* (1996) *J. Cell Biol.* 135:1619-1632 a copy of which is submitted herewith as Appendix A) one of ordinary skill in the art would be able to make such polypeptide fragments using only routine experimentation.

Moreover, Applicants provide detailed teachings in the specification regarding how the skilled artisan would test PCIP of Kv4 potassium channel polypeptides for the identified activities. For example, Applicants teach at page 21, line 24 through page 22, line 4 of the specification how one of skill in the art could test for the ability of a compound to regulate phosphorylation of a potassium channel polypeptide or a PCIP polypeptide. Applicants also teach how one of skill in the art would test for the ability of a compound to modulate the interaction of a potassium channel polypeptide or a PCIP polypeptide with the cytoskeleton (see, for example, page 22, lines 21-26 of the specification). Moreover, in each of the sections cited above, Applicants provide the citations of published manuscripts demonstrating that testing a polypeptide for the specified activities was routine at the time the instant application was filed.

It is a well established principle of patent law that "[t]he specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public." (*In re Buchner* 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991), see also MPEP §2164.05(a)). The structure of the

potassium channel polypeptides identified in the claims was well known to one of ordinary skill in the art at the time the instant application was filed. Moreover, the literature available to the skilled artisan at the time of filing of the instant application would provide guidance as to which potassium channel fragments would be useful in for testing the above-identified activities. The activities highlighted by the Examiner are well known to be carried out by the intracellular portions of the potassium channel polypeptides (see, for example, Murakoshi *et al.* (1997) *Molecular Pharmacology* 52:8221-828 and Jing *et al.* (1997) *J. Biol. Chem.* 272:14021-4, copies of which are submitted herewith as Appendices B and C, respectively). Based on the plethora of available art related to the phosphorylation of other members of the potassium channel family, the skilled artisan would have known that the portions of the Kv4 potassium channels that could be phosphorylated reside in the intracellular portions of the molecule. Moreover, at the time of filing of the instant application, algorithms were available that could accurately predict the portions of a transmembrane polypeptide that are intracellular, extracellular and those segments that are within a membrane (see, for example, Rost *et al.* (1995) *Protein Science* 4:521-533; a copy of which is enclosed herewith as Appendix D).

The test of enablement is not whether any experimentation is necessary, but rather if the experimentation is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). Applicants' teachings in combination with the knowledge available to one of skill in the art would allow the ordinary skilled artisan to practice the claimed invention using only routine, not undue, experimentation. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection and indicate the claims as allowable.

***Rejection of Claims 1, 3, 11-16 Under 35 U.S.C. § 112, Second Paragraph***

The Examiner has rejected claims 1, 3, and 11-16 under 35 U.S.C. § 112, second paragraph as "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Specifically, the Examiner is of the opinion that

[t]he preambles of claims 1, 3 are directed to a method of identifying a compound that binds to and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel. However, the method steps would only identify a compound that binds to and/or modulates the activity of a 9q PCIP polypeptide, and would not necessarily identify a compound that binds to and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel. Thus it is not clear what the method as a whole is

directed to, and the metes and bounds of the claim cannot be determined. Claims 11-16 are rejected insofar as they depend on claim 1, 3.

Solely in the interest of expediting prosecution, and in no way acquiescing to the validity of the Examiner's rejection, Applicants have amended claims 1 and 3 to be directed to methods for identifying a compound that binds to and/or modulates the activity of a Kv4.2 or Kv4.3 potassium channel by binding to and/or modulating the activity of a PCIP polypeptide, thereby rendering this rejection moot. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

**CONCLUSION**

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Applicant believes no fee is due with this statement. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. AHN-069CPRCE from which the undersigned is authorized to draw.

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Respectfully submitted,

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